Principle 7: "No Increased Risk" Threshold for All Tobacco Products

In the absence of any claim of reduced exposure or reduced risk, manufacturers of tobacco products should be permitted to market new products or modify existing products without prior approval of the regulatory agency after informing the agency of the composition of the product and upon certifying that the product could not reasonably be expected to increase the risk of cancer, heart disease, pulmonary disease, adverse reproductive effects, or other adverse health effects, compared to similar conventional tobacco products, as judged on the basis of the most current toxicological and epidemiological information.

Conventional tobacco products are well established in the marketplace, and the committee recognizes that, regardless of the adverse health consequences of using these products, this situation is likely to continue for the foreseeable future. These products are already subject to a limited regulatory system that includes certain health warnings and other labeling requirements and some restrictions on advertising and promotion. The committee considered whether modified versions of established tobacco products, or new brands, that are marketed without health claims should be required, on public health grounds, to satisfy any new regulatory requirements and, if so, whether manufacturers should continue to be permitted to put such conventional products on the market without prior agency approval.

The committee concludes that any new regulatory system should ensure that all newly marketed tobacco products pose no increase in health risks, and ideally a new system should move products toward reduced potential for harm. To this end, the committee recommends that manufacturers be permitted to introduce a new product or make significant changes to an already marketed conventional tobacco product only if, on the basis of currently known toxicological and epidemiological information, the product could not reasonably be expected to increase the risk of disease. Implementation of this regulatory principle requires the definition of a standard for comparison. Although the responsibility for developing such a standard will rest with the regulatory agency, the committee can envision several possibilities: the most popular brand, the most (or least) harmful brand on specified dimensions, a toxicity profile that is representative of a sales-weighted average brand, or a standardized product of known composition. Because toxicant yields do not necessarily reflect health effects and because different standards may be appropriate for different products, the establishment of standards or reference products may require the type of information that would evolve from the regulatory agency's experience with the disclosure of ingredients in individual products (principle 1) and the added-ingredients review (principle 8). Such standards might be promulgated through guidelines and performance standards (principle 9).

To implement this approach, manufacturers should be required, before marketing a product, to submit ingredient information to the agency and to certify that the criterion of no increased risk is met (premarket notification). Whatever comparative standard is adopted for the product, the committee believes that a judgment of no increased risk should be based on the most current toxicological and epidemiological data. Manufacturers should not use the most dangerous products of the past as an appropriate standard for any new product. Consumers should rightfully expect that all new tobacco products, even those marketed without health claims, are at least no more hazardous than similar contemporaneously marketed products.

The committee considered whether premarket approval by the regulatory agency should be required for modifications and new brands of conventional tobacco products without claims of reduced exposure or reduced risk, and rejected this approach in favor of premarket notification and certification by the manufacturer. Although some product modifications may be undertaken

to improve taste or other features linked to consumer satisfaction, future innovation in the tobacco market in this country is likely to focus on changes that purport to reduce risk. Because the main regulatory purpose of a requirement for no increased risk is to help establish the baseline for future comparisons and to stimulate development and use of protocols for tobacco product risk assessment, premarket notification is sufficient. The committee also did not want to see the regulatory agency burdened with a high volume of premarket approval decisions for products that have no claims of and no potential for improving the public health. Nevertheless, the regulatory agency should have the authority to seek the removal of a product from the market in the event that the "no increased risk" standard is not met.

Principle 8: Added-Ingredient Review

All added ingredients in tobacco products, including those already on the market, should be reported to the agency and be subject to a comprehensive toxicological review.

The ingredients added to tobacco products should be subject to a review that is similar to the FDA review of food additives conducted more than two decades ago to determine if those additives were generally recognized as safe and not subject to additional regulation. Although many of the ingredients added to tobacco products are generally recognized as safe when used as food additives, such an understanding may not apply when these substances are combusted and/or inhaled in smoke. A review of added ingredients would establish a baseline of knowledge about the ingredients, including chemicals, papers, and filters, as well as the toxicological testing that has been conducted on them; it would thereby facilitate an informed appraisal of the potential effects of product modifications. This review should be conducted by independent panels of experts reporting to the regulatory agency, with the objective of identifying those ingredients that add no significant toxicity to tobacco products and therefore can be considered safe in the context of this use. Sufficient knowledge of the toxicity of many of the constituents and ingredients of tobacco products may already be available (see Chapter 10) to begin this review. If adequate information is not yet available, the regulatory agency should have the authority to require the in vitro and animal testing that is judged necessary by the expert panels conducting the review. Such a review would begin to rationalize the risk assessment of ingredients in tobacco products;. It would also open this field to the same scientific discourse that is now applied to food additives, environmental contaminants, and toxic chemicals, substances that are no longer introduced into use without independent scientific scrutiny or regulatory review. Tobacco products are the last remaining legally marketed toxic products in our marketplace that are tolerated without such review. A review of added ingredients would provide a scientific basis for guidelines or performance standards to limit possible toxicants like pesticides or filter fibers, if such limits are judged necessary for health reasons. It would also facilitate the review of new products by establishing conditions under which added ingredients, such as flavoring agents and papers, would be considered safe for use without additional data or review.

An added-ingredients review would be a large administrative undertaking requiring several years of effort. It would also require the cooperation of the tobacco industry in submitting data. The committee believes that such a review would be in the interests of both manufacturers and consumers. It would permit credible scientific judgment regarding the extent to which nontobacco ingredients in tobacco products contribute to overall toxicity, would build scientific bridges between the tobacco industry and the toxicology community at large, and as noted above, would facilitate the regulatory review of new products. The committee notes that the review of

food additives has been conducted without public disclosure of trade secrets, such as the composition of spices and flavoring agents, and believes that this principle should be respected in any review of the ingredients added to tobacco products.

Principle 9: Performance Standards

The regulatory agency should be empowered to set performance standards (e.g., maximum levels of toxicants; definitions of terms such as "low tar") for all tobacco products, whether conventional or modified, or for classes of products.

Performance standards, including maximum permissible levels, are promulgated under many regulatory laws, including those related to drugs, medical devices, and environmental pollutants. As noted above, successful implementation of a harm reduction strategy as an element of the nation's tobacco policy will require proactive government efforts in research, education, and surveillance as well as regulation of specific products. Accordingly, as scientific knowledge evolves regarding product risks and consumer preferences, the regulatory authority should be empowered to require product modifications to eliminate unreasonable risks. (A similar recommendation appears in the 1994 IOM report.) The committee has not attempted to draft precise statutory criteria to guide the agency's discretion in adopting performance standards. However, the committee does assume that the agency would not be empowered to ban nicotine from tobacco products.

Performance standards might take the form of limits on the concentrations of toxic ingredients in the product or the smoke; sets of limits that taken together would qualify a smoked product to be labeled as high, average, or low on a risk scale; or a list of reviewed ingredients that could be used without challenging the no increased-risk standard. A performance standard cannot be adopted without good scientific data, deliberate planning, and careful monitoring to ensure that it is achieving the desired goal. As the FTC test for tar and nicotine illustrates, even well intended performance standards can sometimes be subverted, with perverse and unintended health consequences. Performance standards aimed at setting definitions for terms must therefore be thought through with great care and be subject to change as experience is gained. Such standards will undoubtedly require a public rule-making process, meaning considerable time for their adoption.

Principle 10: Enforcement Powers

The regulatory agency should have enforcement powers commensurate with its public health mission, including the power to issue subpoenas.

The committee envisions that any regulatory agency for tobacco-related products would need the usual enforcement authorities conferred on public health regulatory agencies, such as the FDA, FTC, CPSC, and Environmental Protection Agency (EPA). The committee anticipates that this agency would also have an appropriate technical and legal staff concerned with issues of enforcement.

The committee specifically recommends that the agency have among its powers the authority to require the monitoring of scientific studies sponsored by manufacturers and to inspect manufacturers, investigators, and contractors to verify the data submitted in these studies. Such powers are necessary to ensure the quality and integrity of these studies. The agency should also have the authority to remove from the market ingredients or products that do not meet the test of no increased risk; to prohibit claims that are not supported by adequate scientific data; to seize

products that are improperly labeled; to act promptly against advertising campaigns and promotional materials that are false or misleading; and to require corrective action.

Principle 11: Regulation of Drugs and Devices

Exposure reduction claims for drugs that are supported by appropriate scientific and clinical evidence should be allowed by the FDA.

The committee recommends no new legislation regarding the regulation of pharmaceutical products and medical devices intended to assist people to stop smoking. What will be needed is effective policy coordination between FDA regulators responsible for drugs and devices and whatever agency is charged with administering any new legislation related to tobacco products.

The committee also recommends that the FDA be prepared attitudinally and technically to approve both exposure reduction and risk reduction claims for drugs, when such claims are supported by appropriate scientific data. It is clear that the current FDA standard for all approved smoking cessation products is "quit rates" and that long-term use of pharmaceutical PREPs with cigarettes, which might be employed in a harm reduction strategy, is discouraged by the labeling approved for these products (Hughes et al., 1999). While the committee again emphasizes that cessation of smoking is the desired goal for all smokers, it also concludes that drugs with exposure reduction and risk reduction claims, if properly regulated and proved efficacious, have a place among the treatment modalities that should be available to current smokers. The committee judges, for example, that statements such as "helps recruitment into treatment clinics" or "reduces the use of cigarettes without compensation" are appropriate indications if supported by adequate data from clinical trials. The committee also concludes that for persons addicted to nicotine, a nicotine-containing drug product is preferable to a cigarette or other tobacco-containing product as a chronic source of nicotine. The FDA should therefore be prepared to consider the chronic administration of nicotine products as a reasonable exposure reduction strategy, again if supported by valid clinical data

Although the committee believes that adequate regulation of tobacco-related PREPs requires new legislation conforming to the preceding principles, the potential utility of the existing authority of the FDA and FTC should not be overlooked, and some of the committee's recommendations could be implemented by these agencies in the absence of new authority. The FDA presently has the authority to regulate any product, including new or existing tobacco products, as drug-delivery devices or as drugs on the basis of an expressed or implied claim by the manufacturer that the product prevents disease by reducing the health risks of tobacco (Page, 1998). FDA can find that a manufacturer intends to make such a claim by looking at any relevant source, including advertising. See United States v. "Sudden Change,"(United States v. "Sudden Change," 1969), and National Nutritional Foods Assn. v. FDA (National Nutritional Foods Assn. v. FDA), (objective evidence). Claims that PREPs respond to concerns about smoking-related illnesses or cancer can be regarded as disease prevention claims.

In its recommendations for regulating the risk reduction claims for PREPs, this report identifies the type of testing and post-approval studies that should be conducted. The committee recommends that FDA use these testing standards under its existing authority in regulating PREPs that make claims for reduced risk of disease. FDA can regulate products that are both drugs and devices under its authority over medical devices. In the case of medical devices that require premarket approval, the agency can determine what testing needs to be done to provide a "reasonable assurance" of safety and effectiveness and can set performance standards for class II devices where appropriate (21 U.S.C.; Page, 1998). The products can be considered safe on a

relative basis in light of their capacity for risk reduction, even though tobacco itself was not considered safe in FDA v. Brown & Williamson (LII, 2000). Post-approval testing has been allowed and required for new drugs (Page, 1998).

Exposure reduction claims, such as low tar, have not been regulated by FDA as disease claims, and its authority to do so is uncertain (Page, 1998). A new law designed specifically to regulate tobacco-related PREPs can give a regulatory agency clear authority with respect to exposure-related and smokeless claims. Even for disease prevention claims, new legislation can confirm the agency's authority and the type of tests and manner in which the agency should regulate claims. Moreover, the legislation recommended by the committee would provide the agency new authority to obtain data on ingredients of all tobacco products, permit additional disclosures to consumers about toxicants in tobacco, give enhanced authority (and review when needed) over advertising and labeling claims for PREPs, guard against increased risks from new or modified tobacco products, and authorize a toxicology review and performance standards for tobacco products.

FDA's authority with respect to disease claims would continue if the new authority recommended under this report were given to FDA, with whatever modifications were made by statute. If the authority were given to a new agency, FDA's authority over disease claims for PREPs should be revoked only if the new agency has authority that is at least as extensive as FDA's present authority.

SUMMARY

In this chapter, the committee has addressed key elements of a regulatory framework for implementing the scientific and policy recommendations made in the body of the report. In the committee's judgment, harm reduction is a feasible and justifiable public health policy—but only if it is implemented carefully to achieve the following objectives:

- Manufacturers have the necessary incentive to develop and market products that reduce exposure to tobacco toxicants and that have a reasonable prospect of reducing the risk of tobacco-related disease;
- Consumers are fully and accurately informed of all of the known, likely, and potential consequences of using these products;
- Promotion, advertising and labeling of these products are firmly regulated to prevent false or misleading health claims, whether these claims are explicit or implicit;
- Health and behavioral effects of all PREP use are monitored on a continuing basis;
- Basic, clinical, and epidemiological research is conducted to establish with reasonable scientific certainty the actual health benefits of PREPs to individuals and the population as a whole; and
- Harm reduction is implemented as a component of a comprehensive national tobacco control program that emphasizes abstinence-oriented prevention and treatment.

The committee nevertheless acknowledges that a regulatory system of the type outlined in this report will require sustained congressional support and substantial public funding. It will also impose new direct and indirect costs on the tobacco industry. The committee emphasizes, however, that the regulatory system proposed in this report is not to be viewed in isolation. It is proposed as an essential component of a package of public policy initiatives (including research, education and surveillance) that this committee believes is necessary to realize whatever benefit

tobacco or pharmaceutical product innovation can offer in reducing the nation's burden of tobacco-related illness and death. The committee notes again that public health benefits may not emerge, even if the public and private investment in these initiatives is made. In the absence of this investment, however, the hoped-for benefits are highly unlikely to materialize.

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